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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

ANDERSON, JAMES D

ART UNIT

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1614

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/532,041	Applicant(s) SCHUTZE ET AL.	
	Examiner JAMES D. ANDERSON	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-9,11,14,15 and 18-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-9,11,14,15 and 18-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/21/2005 and 5/2/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-9 and 11-21 are presented for examination

Election/Restrictions

Applicant's election of celecoxib as the anti-inflammatory agent in the reply filed on 3/6/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3-4, 12-13, and 16-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/6/2008.

Accordingly, pursuant to Applicants' election of celecoxib, claims 1-2, 5-9, 11, 14-15, and 18-21 read on the elected species and are presently under examination.

Priority

The present application is a 371 of PCT/FR03/03120, filed 10/21/2003 and claims foreign priority to FR 02/13115, filed 10/21/2002.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statements filed on 4/21/2005 and 5/2/2007. The Examiner has considered the references cited therein to the extent that each is a proper citation. The International Search Report filed in the 4/21/2005 IDS was not considered because search reports are not considered "published" documents by the USPTO. Please refer to the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 11, 14, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation "is comprised between" as recited in claims 6, 11, and 14 is unclear when used in relation to the claimed weight ratio ranges. It is not clear whether it is Applicants' intent that the weight ratio be specifically between the claimed ranges, or whether the claimed ranges are only part of ("comprised") a broader range. Amending the claims to recite "is between" would overcome this rejection provided there is support in the specification for such an amendment.

Claims 9 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation "*is administrable* via the oral or the parenteral route" as recited in the instant claims renders the claims indefinite because it is not clear whether this

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limitation results in a material change in the compositions. For example, a pharmaceutical composition comprising tenatoprazole and celecoxib in a topical cream "is administrable" via the oral route (*i.e.*, one is capable of ingesting a topical cream), but is structurally and materially different than a composition comprising tenatoprazole and celecoxib in tablet form.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5-9, 11, 14-15, 18-19, and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Brulls** (USP No. 6,730,685 B1; Issued May 4, 2004; Filed Oct. 13, 2000) (newly cited) in view of **Mangel *et al.*** (WO 01/56573 A1; Published August 9, 2001) (prior art of record).

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Brulls teaches pharmaceutical compositions that are combinations of tenatoprazole and other drug treatments, such as “a motility stimulating drug” (column 7, lines 22-26).

Tenatoprazole is exemplified as a compound of Formula I at the top of column 12. Brulls' teaching is drawn to treatment of diseases relating to gastric hyperacidity, such as gastric and duodenal ulcers and reflux esophagitis (columns 6-7 under Use of the Invention). A dosage range for tenatoprazole is taught to be 1-100 mg once or twice a day (column 7, lines 14-15). Both oral and parenteral administration is disclosed in column 3, lines 1-8. As required by instant claim 8, sodium or potassium salts are disclosed in claims 4 and 5. Brulls is silent with respect to the disclosed “motility stimulating drug”.

However, Mangel *et al.* teach using COX-2 inhibitors for the treatment of disorders ameliorated by a gastroprokinetic, based on the discovery that COX-2 inhibitors stimulate gastrointestinal motility (Abstract; page 1, lines 29-30). Celecoxib (as elected by Applicants) is among the COX-2 inhibitors disclosed for use in the invention taught in Mangel *et al.* (page 5, line 7; page 7, line 14; page 8, line 4). With respect to tenatoprazole, Mangel *et al.* teach that it may be advantageous to administer other therapeutic agents in combination with a COX-2 inhibitor (page 8, lines 10-12); among such agents are proton pump inhibitors, specifically tenatoprazole (page 8, lines 15-17). With respect to the dose of celecoxib as recited in claims 7, 15, 18, and 19, Mangel *et al.* suggest effective doses of the COX-2 inhibitors of the invention are 0.01 to 500 mg, preferably 0.05 to 250 mg, for example 0.5 to 100 mg per unit dose (page 11, lines 8-11). With respect to compositions being administrable via the oral or the parenteral route as recited in claims 9 and 20, Mangel *et al.* teach that the compositions of the invention can be formulated for oral or parenteral administration (page 9, lines 9-15).

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Brulls and Mangel *et al.* thus suggest and motivate combining a “motility stimulating drug” (*e.g.*, celecoxib) with a proton pump inhibitor (*e.g.*, tenatoprazole).

Brulls and Mangel *et al.* differ from the compositions as recited in the instant claims in that they do not disclose the weight ratio of tenatoprazole to anti-inflammatory agent (*e.g.*, celecoxib) as recited in claims 6, 11, and 14. However, it would have been obvious to one of ordinary skill in the art at the time of the invention that the ratio of tenatoprazole to celecoxib could be readily adjusted in order to formulate a composition for the treatment of diseases ameliorated by a gastroprokinetic as suggested by Mangel *et al.* Such optimization of a prior art composition suggested by the prior art is well within the purview of the skilled artisan and could be achieved through routine experimentation. It is not inventive to discover an optimum or workable range by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(II). The currently claimed specific weight ratio ranges are not seen to be inconsistent with ranges that would have been readily determined by the skilled artisan via routine optimization.

Claims 1-2, 5-7, 9, 11, 14-15, 18-19, and 20-21 rejected under 35 U.S.C. 103(a) as being unpatentable over **Chih-Ming *et al.*** (WO 02/22108 A1; Published March 21, 2002) (prior art of record) in view of **Mangel *et al.*** and **Naesdal *et al.*** (European Journal of Gastroenterology and Hepatology, 2001, vol. 13, pages 1401-1406) (newly cited).

Chih-Ming *et al.* teach oral solid dosage forms containing a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor effective to inhibit or prevent gastrointestinal side effects normally associated with the NSAID (Abstract). With respect to

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NSAIDs, Chih-Ming *et al.* teach that “NSAID” refers to “any compound acting as a non-steroidal anti-inflammatory agent identifiable as such by one of ordinary skill in the art” (page 9). With respect to tenatoprazole, Chih-Ming *et al.* teach that any proton-pump inhibitor may be used in the invention disclosed therein, but they do not explicitly recite the claimed tenatoprazole (pages 10-11). However, the inventors do suggest that isomers, enantiomers, tautomers, and alkaline salts of proton pump inhibitors may be used (page 11), and that the compositions comprising a NSAID and proton pump inhibitor is administered orally (page 12). In preferred examples, the weight ratio of proton pump inhibitor to NSAID is about 1:10 or 1:5, thus suggesting the limitations of claims 6, 11, and 14 (pages 27-31)

Chih-Ming *et al.* differ from the instant claims in that they do not specify tenatoprazole as a proton-pump inhibitor of the invention and they do not teach that the NSAID can be celecoxib.

However, Mangel *et al.*, as discussed *supra*, teach that it may be advantageous to administer other therapeutic agents in combination with a COX-2 inhibitor (page 8, lines 10-12); among such agents are proton pump inhibitors, specifically tenatoprazole (page 8, lines 15-17).

Further, Naesdal *et al.* provide additional motivation to administer a proton pump inhibitor to patients being treated with a COX-2-selective NSAID. In this regard, Naesdal *et al.* teach that while COX-2-selective NSAIDs are associated with a lower risk of ulceration than non-selective NSAIDs, comparable proportions of NSAID users report upper gastrointestinal symptoms regardless of COX- selectivity (Abstract; page 1404, right column)). The authors thus suggest that a proton pump inhibitor should be considered for prevention of ulceration associated with NSAID use (*id.*).

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Accordingly, in view of the cited prior art, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine tenatoprazole and celecoxib in a pharmaceutical composition. As discussed *supra*, Chih-Ming *et al.* suggest and motivate the combination of a NSAID and a proton-pump inhibitor generally, although they do not explicitly teach the claimed tenatoprazole and celecoxib. However, tenatoprazole was a well-known proton-pump inhibitor at the time of the invention as evidenced by Mangel *et al.* and thus one skilled in the art would recognize that tenatoprazole would be useful as a proton-pump inhibitor in the invention disclosed in Chih-Ming *et al.* With respect to celecoxib, although the prior art recognizes that use of celecoxib is accompanied by fewer gastrointestinal side effects when compared to non-selective NSAIDs (see Naesdal *et al.*), the prior art also suggests that proton pump inhibitors should be considered for prevention of ulceration associated with NSAID use generally (*id.*). As such, the skilled artisan would have been imbued with at least a reasonable expectation that a pharmaceutical composition comprising tenatoprazole and celecoxib would be useful in the treatment of pain and inflammation and would potentially result in fewer gastrointestinal side effects as suggested by Chih-Ming *et al.* in view of Mangel *et al.* and Naesdal *et al.*

Claims 1-2, 5-9, 11, 14-15, 18-19, and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Chih-Ming *et al.***, **Mangel *et al.***, **Naesdal *et al.*** as applied to claims 1-2, 5-7, 9, 11, 14-15, 18-19, and 20-21 above, and further in view of **Bergstrand *et al.*** (USP No. 5,753,265; Issued May 19, 1998) (newly cited).

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Chih-Ming *et al.*, Mangel *et al.*, and Naesdal *et al.* teachings are discussed supra and are applied herein in the same manner and in their entirety. Claim 8 differs from Chih-Ming *et al.*, Mangel *et al.*, and Naesdal *et al.* in that the references do not disclose the specific alkaline salts of tenatoprazole recited in the claim.

However, Bergstrand *et al.* teach pharmaceutical preparations containing an acid labile H^+K^+ -ATPase inhibitor or an alkaline salt thereof (Abstract). Tenatoprazole is one such acid labile H^+K^+ -ATPase inhibitor as disclosed at column 3, lines 20-25. The alkaline salts recited in instant claim 8 are taught at column 3, lines 36-39. The compounds of the invention are taught to be useful in inhibiting gastric acid secretion in mammals and for the treatment of gastrointestinal disorders where gastric acid inhibitory effect is desirable, *e.g.*, in patients on NSAID therapy (*id.* at lines 44-52).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use an alkaline salt of tenatoprazole in the pharmaceutical formulations suggested by the cited prior. The motivation to do so is found in Bergstrand *et al.*, who teach that such alkaline salts are useful in pharmaceutical preparations for the treatment of gastrointestinal disorders.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Chan *et al.* (N. Engl. J. Med., Dec. 2002, vol. 347, no. 26, pages 2104-2110) teach that celecoxib when compared to diclofenac and omeprazole has the same incidence of recurrent ulcer bleeding (Abstract) and thus suggest that combinations of a COX-2 selective NSAID with a

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proton-pump inhibitor should be studied to assess whether such combinations will eliminate the risk of ulcer complications for patients with multiple risk factors.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614